We have communicated with the public and manufacturers of FDA-regulated products about appropriate steps to increase product safety and minimize the risk of products contaminated with the BSE agent. We published a notice in the Federal Register of August 29, 1994 (59 FR 44592), entitled ``Bovine-Derived Materials; Agency Letters to Manufacturers of FDA-Regulated Products'' (Ref. 50). The notice, in part, published the November 1992 and December 1993 letters to manufacturers. In November 1992, we wrote to manufacturers of dietary supplements to alert them to the developing concern about TSEs in animals and Creutzfeldt-Jakob Disease in humans and recommended that they investigate the geographic source of any bovine and ovine material used in their products. We suggested that manufacturers develop plans to ensure, with a high degree of certainty, that bovine and ovine materials used in their products were not from BSE countries or from sheep flocks (foreign or domestic) infected with scrapie. In December 1993, we issued a letter recommending against the use of bovine-derived materials from cattle that resided in, or originated from, BSE countries in FDA-regulated products. In this letter, we recommended that manufacturers: (1) Identify bovine-derived materials in their products and identify all countries where the animals used to produce the materials had lived, (2) maintain traceable records for each lot of bovine materials and for each lot of FDA-regulated product using these materials, (3) document the country of origin of the live animal source of any bovine-derived materials used in the manufacture of the regulated products, and (4) maintain copies of the records identified above for FDA-regulated products manufactured using bovine-derivec materials at foreign sites or by foreign manufacturers. To assure the safety and suitability for human use of animal-derived biologics, our Center for

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Biologics Evaluation and Research (CBER) has developed guidances for industry that describe steps that manufacturers should take. For example, CBER guidances have recommendations that address viral safety, infections, disease risks, and BSE-risk reduction of biologic products that are animal-derived (see 63 FR 51074, September 24, 1998, and 63 FR

50244, September 21, 1998) (Refs. 51 and 52). Because we believe that the use of an animal-derived material, substance, or tissue in a dietary supplement may raise many of the same serious public health and safety issues as animal-derived materials, substances, or tissues, in a biologic, we are considering whether the procedures that CBER recommends for a product with animal-derived materials, substances, or tissues would be appropriate for dietary ingredients and dietary supplements that contain animal-derived materials, substances, or tissues. We, therefore, invite comment on whether there should be specific CGMP requirements for the use of animal-derived materials, substances, or tissues in dietary ingredients and dietary supplements. We invite comment on these issues and specifically on whether there is a scientific basis for FDA to treat animal-derived dietary ingredients in a manner that is different from, or that would offer less protection than, what is recommended for animal-derived biologics when the same public health and safety risks may be present. We also invite comment on our legal authority with respect to these issues.

5. Exclusions (Proposed Sec. 111.6)

Proposed Sec. 111.6 would state that these CGMP regulations do not apply to a person engaged solely in activities related to the harvesting, storage, or distribution of raw agricultural commodities that will be incorporated into a dietary ingredient or dietary supplement by other persons. This proposed exclusion is similar to the exclusion in Sec. 110.19 for raw agricultural commodities. Accordingly, persons who engage in such activities related to raw agricultural commodities (which are defined in section 201(r) of the act), although not subject to these proposed CGMP regulations under section 402(g) of the act, would continue to be subject to other adulteration provisions in section 402 of the act.

We recognize that including in the proposed rule persons who engage in the activities related to the harvesting, storage, or distribution of such commodities, as described previously, could reduce the risk of microbial contamination in dietary ingredients and dietary supplements. Nevertheless, the proposal does not contain requirements for persons handling such commodities before distribution to a dietary ingredient or dietary supplement manufacturer because the scientific basis for reducing or eliminating pathogens in various settings is evolving. We